erythromelalgia

Erythromelalgia is a condition characterized by episodes of pain, redness, and swelling in various parts of the body, particularly the hands and feet. These episodes are usually triggered by increased body temperature, which may be caused by exercise or entering a warm room. Ingesting alcohol or spicy foods may also trigger an episode. Wearing warm socks, tight shoes, or gloves can cause a pain episode so debilitating that it can impede everyday activities such as wearing shoes and walking. Pain episodes can prevent an affected person from going to school or work regularly.

The signs and symptoms of erythromelalgia typically begin in childhood, although mildly affected individuals may have their first pain episode later in life. As individuals with erythromelalgia get older and the disease progresses, the hands and feet may be constantly red, and the affected areas can extend from the hands to the arms, shoulders, and face, and from the feet to the entire legs.

Erythromelalgia is often considered a form of peripheral neuropathy because it affects the peripheral nervous system, which connects the brain and spinal cord to muscles and to cells that detect sensations such as touch, smell, and pain.

Frequency

The prevalence of erythromelalgia is unknown.

Genetic Changes

Mutations in the *SCN9A* gene can cause erythromelalgia. The *SCN9A* gene provides instructions for making one part (the alpha subunit) of a sodium channel called NaV1.7. Sodium channels transport positively charged sodium atoms (sodium ions) into cells and play a key role in a cell's ability to generate and transmit electrical signals. NaV1.7 sodium channels are found in nerve cells called nociceptors that transmit pain signals to the spinal cord and brain.

The *SCN9A* gene mutations that cause erythromelalgia result in NaV1.7 sodium channels that open more easily than usual and stays open longer than normal, increasing the flow of sodium ions into nociceptors. This increase in sodium ions enhances transmission of pain signals, leading to the signs and symptoms of erythromelalgia. It is unknown why the pain episodes associated with erythromelalgia mainly occur in the hands and feet.

An estimated 15 percent of cases of erythromelalgia are caused by mutations in the *SCN9A* gene. Other cases are thought to have a nongenetic cause or may be caused by mutations in one or more as-yet unidentified genes.

Inheritance Pattern

Some cases of erythromelalgia occur in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some of these instances, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- erythermalgia
- familial erythromelalgia
- primary erythromelalgia

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Primary erythromelalgia
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0014805/

Other Diagnosis and Management Resources

- GeneReview: SCN9A-Related Inherited Erythromelalgia
  https://www.ncbi.nlm.nih.gov/books/NBK1163

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Pain
  https://medlineplus.gov/pain.html
- Health Topic: Peripheral Nerve Disorders
  https://medlineplus.gov/peripheralnervedisorders.html

Genetic and Rare Diseases Information Center

- Erythromelalgia
  https://rarediseases.info.nih.gov/diseases/6377/erythromelalgia

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Chronic Pain Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Chronic-pain-Information-Page
- National Institute of Neurological Disorders and Stroke: Peripheral Neuropathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Peripheral-Neuropathy-Information-Page

Educational Resources

- Cleveland Clinic: Neuropathy
  http://my.clevelandclinic.org/health/articles/neuropathy
- Disease InfoSearch: Erythromelalgia, Primary
  http://www.diseaseinfosearch.org/Erythromelalgia%2C+Primary/2646
- Johns Hopkins Medicine: Peripheral Neuropathy
  http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/nervous_system_disorders/peripheral_neuropathy_134,51/
- MalaCards: erythromelalgia
  http://www.malacards.org/card/erythromelalgia
- Merck Manual Consumer Version
  http://www.merckmanuals.com/home/heart-and-blood-vessel-disorders/peripheral-arterial-disease/erythromelalgia
- Merck Manual Consumer Version: Nociceptive Pain
  http://www.merckmanuals.com/home/brain,-spinal-cord,-and-nerve-disorders/pain/nociceptive-pain

- Orphanet: Erythromelalgia
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1956
- Washington University, St. Louis: Neuromuscular Disease Center
  http://neuromuscular.wustl.edu/sensory-pain.html#erythromelalgia

Patient Support and Advocacy Resources

- American Chronic Pain Association
  https://theacpa.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/erythromelalgia/
- The Erythromelalgia Association
  http://www.erythromelalgia.org/
- The Foundation for Peripheral Neuropathy
  https://www.foundationforpn.org/

GeneReviews

- SCN9A-Related Inherited Erythromelalgia
  https://www.ncbi.nlm.nih.gov/books/NBK1163

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22erythromelalgia%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28erythromelalgia%5BTIAB%5D%29+OR+%28erythermalgia%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ERYTHERMALGIA, PRIMARY
  http://omim.org/entry/133020

Sources for This Summary

- Cregg R, Laguda B, Werdehausen R, Cox JJ, Linley JE, Ramirez JD, Bodi I, Markiewicz M, Howell KJ, Chen YC, Agnew K, Houlden H, Lunn MP, Bennett DL, Wood JN, Kinali M. Novel mutations mapping to the fourth sodium channel domain of Nav1.7 result in variable clinical manifestations of primary erythromelalgia. Neuromolecular Med. 2013 Jun;15(2):265-78. doi: 10.1007/s12017-012-8216-8. Epub 2013 Jan 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23292638
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3650253/
- Dib-Hajj SD, Cummins TR, Black JA, Waxman SG. From genes to pain: Na v 1.7 and human pain disorders. Trends Neurosci. 2007 Nov;30(11):555-63. Epub 2007 Oct 22. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17950472
- Dib-Hajj SD, Cummins TR, Black JA, Waxman SG. Sodium channels in normal and pathological pain. Annu Rev Neurosci. 2010;33:325-47. doi: 10.1146/annurev-neuro-060909-153234. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20367448
- Drenth JP, te Morsche RH, Guillet G, Taieb A, Kirby RL, Jansen JB. SCN9A mutations define primary erythermalgia as a neuropathic disorder of voltage gated sodium channels. J Invest Dermatol. 2005 Jun;124(6):1333-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15955112
- Emery EC, Habib AM, Cox JJ, Nicholas AK, Gribble FM, Woods CG, Reimann F. Novel SCN9A mutations underlying extreme pain phenotypes: unexpected electrophysiological and clinical phenotype correlations. J Neurosci. 2015 May 20;35(20):7674-81. doi: 10.1523/JNEUROSCI.3935-14.2015.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25995458
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4438121/
- Estacion M, Han C, Choi JS, Hoeijmakers JG, Lauria G, Drenth JP, Gerrits MM, Dib-Hajj SD, Faber CG, Merkies IS, Waxman SG. Intra- and interfamily phenotypic diversity in pain syndromes associated with a gain-of-function variant of NaV1.7. Mol Pain. 2011 Dec 2;7:92. doi: 10.1186/1744-8069-7-92.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22136189
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3248882/
- Han C, Dib-Hajj SD, Lin Z, Li Y, Eastman EM, Tyrrell L, Cao X, Yang Y, Waxman SG. Early- and late-onset inherited erythromelalgia: genotype-phenotype correlation. Brain. 2009 Jul;132(Pt 7):1711-22. doi: 10.1093/brain/awp078. Epub 2009 Apr 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19369487
- Waxman SG, Dib-Hajj S. Erythermalgia: molecular basis for an inherited pain syndrome. Trends Mol Med. 2005 Dec;11(12):555-62. Epub 2005 Nov 8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16278094

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/erythromelalgia

Reviewed: February 2016
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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